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14. ABSTRACT
A prospective/longitudinal design examined the effects of OIF-related emotion symptoms and mTBI exposure on post deployment function. Both performance-based and self-report outcome measures were collected. Regression analytic strategies examined post-OIF function on objective neurocognitive measures and self reported cognitive and physical problems, measuring the predictive contribution of self-report of mild TBI; self-report regarding emotional function immediately post-deployment (e.g., symptoms of posttraumatic stress disorder [PTSD] and depression); and self-reported combat exposure. This study demonstrates a clear relationship between deployment-related emotional functioning and post-OIF cognition; results failed to indicate a similar mTBI/cognition relation, but nonetheless provided some evidence of a relationship between mTBI and post-OIF outcome.

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Introduction

Mild traumatic brain injury (mTBI) is thought to be common among service members returning from OIF war-zone deployment. Recent studies have conducted preliminary examinations of mTBI exposure and OIF-related emotion symptom effects on post deployment function (Hoge, 2008; Vanderploeg et al., 2009), but understanding of these relationships remains incomplete. Major knowledge gaps include minimal war-zone data documenting mTBI exposure, assessments conducted long after war-zone exposure, dependence on self-report of cognitive function, and the absence of prospectively gathered pre-deployment data allowing examination of change in relevant outcomes over time. Cognitive impairment is a functionally relevant but understudied outcome of war, figuring prominently among veteran health complaints after past military conflicts (Department of Veterans Affairs, VHA, Office of the Assistant Secretary of Defense, Health Affairs, 2002). The Neurocognition Deployment Health Study (NDHS) is a prospective cohort-controlled design measuring subjective and objective neurocognitive outcomes in Army soldiers deployed to Iraq. In this research, we examine deployment-related changes in cognition in the Active Duty subset of NDHS participants. Our research had two aims: to examine pre-deployment variable that might serve as predictors of deployment interval mTBI (**Aim 1**), and to examine the relative effects of OIF–related emotion symptoms, self report of relevant deployment-related stressors, and self-reported mTBI exposure on performance-based cognitive outcomes after military deployment to Iraq (**Aim 2**).

Body

Sample. Military units at high likelihood of deployment to Iraq were assessed prior to deployment (Time 1, between April and December 2003) and again following their return (Time 2, between January and May 2005). Soldiers that were initially seen as control subjects but later deployed were also tested post-deployment; these soldiers were also included in the analyses. See Vasterling et al. (2006a, 2006b) for details regarding sampling rationale and characteristics. Subjects were 780 active duty soldiers who deployed to Iraq, with pre (Time 1) and post (Time 2) deployment data on relevant neurocognitive measures. Of this sample, 70 soldiers reported a deployment interval TBI that led to a distinct loss of consciousness, and 87 soldiers scored above a PTSD Checklist (PCL) cutoff of 50 + DSM symptom congruency for deployment related PTSD.

Aim 1: prediction of deployment interval mTBI. To maximize the likelihood of capturing relevant mTBI-predictor relationships, uncontrolled chi-square and t-test analyses were conducted examining the statistical relationship between deployment related mTBI and a variety of relevant predeployment variables. For all analyses, the grouping variable was report of a deployment interval head injury (i.e., yes/no). Categorical predictors examined via chi-square analysis included gender, ethnicity, marital status, educational degree (GED or higher), handedness, diagnosis of ADHD, diagnosis of learning disability, and history of pre-deployment head injury. Demographic continuous predictors examined via t-test included education level, rank, and average reported pre-deployment sleep level. Self report continuous measures included predeployment subscales of the Deployment Risk and Resilience Inventory (DRRI: see King et al., 2006, for details regarding this measure). DRRI subscales examined included pre-deployment family concerns, exposure to pre-deployment stressors, leadership and unit cohesion appraisal, and training quality appraisal.

Aim 1 Results. Two categorical predictors reached conventional significance levels (i.e., $p \leq .05$): gender ($X^2 = 4.47$, $\underline{p} = .035$); and history of pre-deployment head injury ($X^2 = 5.75$, $\underline{p} = .017$). Gender differences imply that male soldiers from this sample reported higher rates of deployment-related mTBI; this result likely reflects a greater probability of male assignment to combat-related duties. Pre-deployment head injury in this sample serves as a risk factor predicting greater likelihood of a subsequent deployment-related head injury and is consistent with findings in the civilian TBI literature. All other

categorical predictors did not reach significance (p values ranging from .275 to .870). No continuous predictors, either demographic or based on DRRI measures, reached significance, with p values ranging from .072 to .818. The only continuous predictor to approach significance was the DRRI subscale measuring training quality, with head injured soldiers indicating slightly higher appraisals of training quality than non-head injured soldiers. Follow-up examinations utilizing logistic regression were conducted to identify possible subsets of cognitive or demographic variables could be identified to enhance prediction of deployment period head injury. No predictors reached significance.

Aim 2: Relative contribution of mTBI, emotion outcome, and combat exposure to prediction of cognitive outcomes. Hierarchical regression was used to examine to examine the relative contributions of a variety of variables to prediction of fourteen different cognitive outcomes and two self-reported health outcomes. All relevant variables are listed in the Measures table (Table 1). A set of control variables included initial (Time 1) levels of outcomes; demographics (age, education); and situational factors (recent alcohol use, test-retest interval). To test for a recently predicted relationship between mTBI and stress disorders (Bryant, 2008), a statistical interaction effect was also included in all regression tests.

Model: Hierarchical regression.
Outcome measures: Time 2/post deployment neurocognitive function (see Measures for details)

- Step 1: relevant Time 1/pre deployment measure, i.e., autoregressor
- Step 2: demographics and situational factors
- Step 3: mTBI status
- Step 4: emotional status as measured by PTSD (Model 1), depression symptoms (Model 2), and DRRI (Model 3)
- Step 5: mTBI x Model variable (e.g., PTSD, depression, DRRI) interaction.

Aim 2 Results. PTSD status is a reliable predictor of a broad range of cognitive changes associated with OIF deployment; the presence of PTSD is associated with deficits in fine motor speed, cognitive efficiency, visual learning and memory, verbal learning, and self-reported health and cognitive problems. (See Table 2 for all results.) This relationship holds even when statistical controls are exerted for pre-OIF cognitive function (this regression term was in all cases significant), theoretically relevant demographic and control variables, the independent effects of mTBI, and potential mTBI/PTSD interaction effects. This pattern of results is very closely replicated when self-report of depression symptoms is substituted for PTSD as a predictor. Report of combat exposure does not serve as a significant predictor of cognitive outcome. Self report of exposure to mTBI, as measured in this study, is also not a reliable predictor of neurocognitive outcome, regardless of whether or not PTSD or depression symptoms are accounted for statistically. Regarding subjective perceptions of outcome, mTBI contributes significantly and independently to prediction of self-reported post-OIF health-related functioning, but not to self-report of cognitive deficit. No analyses produced significant mTBI/PTSD, mTBI/depression, or mTBI/DRRI interactions.

To further investigate the relative contribution of mTBI to cognitive outcome, four alternative analytic procedures were considered:

1) Exploration of creation of a continuous index of mTBI by incorporating self-report of number of mild TBI incidents and estimated loss of consciousness time spans;
2) Reanalysis using only subjects who clearly reported a combat related mTBI during the deployment interval;
3) Reanalysis comparing mTBI to a dichotomous measure of PTSD;
4) Reanalysis using additional demographic control variables such as race and reported pre-test sleep.

These alternative procedures were considered singly and in some combinations for all regressions reported in Table 2. In all cases, use of these alternative strategies yielded results substantively equivalent to those just reported; PTSD and depression measures were significant predictors of cognitive outcome, while mTBI and combat exposure failed to demonstrate reliable predictive validity.

Key Research Accomplishments

- A demonstration that self-reported deployment-related PTSD symptoms significantly predicts objectively-measured cognitive outcome in a variety of functional domains.
- This relationship holds despite controlling for related pre-deployment cognitive function and a variety of other potentially confounding demographic and situational factors.
- A demonstration that a similar relationship exists with a related measure of depression.
- While mTBI was not a significant predictor of cognitive problems, it proved to be a significant predictor of self-reported physical health problems, even after controlling for the relative predictive contribution of PTSD or depression.

Reportable Outcomes

Brailey, K., Vasterling, J. J., Proctor, S. P., Amoroso, P., White, R. F., & Kane, R. (2009, September). *MTBI and emotion symptom effects on neurocognitive performance: a longitudinal study of OIF deployed Army soldiers*. Invited presentation at the Annual Military Health Research Forum, Kansas City, Missouri.

Manuscript under preparation describing results related to Aim 2.

Conclusions

A survey of predeployment factors failed to uncover any reliable predictors of deployment related mild TBI beyond previous occurrence of related TBI. Regression analyses utilizing self-report of PTSD indicate that symptoms of deployment related emotional distress are significantly related to post-deployment cognitive outcome. The existence of an analogous depression-cognitive outcome suggests that the impact of deployment is not related strictly to PTSD and instead reflects more global levels of emotional distress.

Mild traumatic brain injury (mTBI) was not a significant predictor of cognitive outcome in this sample, despite use of liberal exploratory techniques designed to maximize the likelihood of uncovering meaningful mTBI-cognition effects. However, a significant mTBI/physical complaints relationship suggests that mTBI may be exerting a deleterious effect on readjustment of deployed troops. This relationship is unlikely to be due solely to demand characteristics, since no relationship was found between mTBI and self report of cognitive complaints. The congruence between cognitive objective performance and cognitive self-report data in this sample instead is consistent with the possibility that simple self report of mTBI is tapping a distress factor with unclear consequences. Improved reliability of mTBI measures would assist in further delineating this potential relationship.

References

Bryant, R. A. (2008). Disentangling mild traumatic brain injury and stress reaction. *The New England Journal of Medicine, 358,* 525-527.

Department of Veterans Affairs, VHA, Office of the Assistant Secretary of Defense, Health Affairs (VA and DOD). (2002). *Combined Analysis of the VA and DoD Gulf War Clinical Evaluation*

Programs: a Study of the Clinical Findings from Systematic Medical Examinations of 100,339 U.S. Gulf War Veterans. Washington, DC.

Hoge, C. W. (2008). Mild traumatic brain injury in U.S soldiers returning from Iraq. *The New England Journal of Medicine, 358,* 453-463.

Hoge, C. W., Castro, C. A., Messer, S. C., McGurk, D., Cotting, D. I., & Koffman, R. L. (2004). Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *New England Journal of Medicine, 351*(1), 13-22.

King, D. W., King, L. A., Vogt, D. S., Knight, J., & Samper, R. E. (2006). Deployment Risk and Resilience Inventory: A collection of measures for studying deployment-related experiences of military personnel and veterans. *Military Psychology, 18,* 89-120.

Vanderploeg, R.D., Belanger, H.G., & Curtiss, G. (2009). Mild traumatic brain injury and posttraumatic stress disorder and their associations with health symptoms. *Archives of Physical and Medical Rehabilitation, 90(7),* 1084-93.

Vasterling, J. J., & Brailey, K. (2005). Neuropsychological Findings in Adults with PTSD. In *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives.* (pp. 178-207). New York, NY, US: Guilford Press.

Vasterling, J. J., Proctor, S. P., Amoroso, P., Kane, R., Heeren, T., & White, R. F. (2006b). Neuropsychological outcomes of army personnel following deployment to the Iraq war. *JAMA, 296*(5), 519-529.

Vasterling, J. J., Proctor, S. P., Amoroso, P., Kane, R., Gackstetter, G., Ryan, M. A. K., & Friedman, M. J. (2006a). The neurocognition deployment health study: A prospective cohort study of Army Soldiers. *Military Medicine, 171*, 253-260.

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Table 1. Measures

Predictor measures		
	Instrument	**Domain Assessed**
	PCL	Self-reported posttraumatic stress disorder symptoms
	mTBI	Self-reported occurrence of acute incident (e.g., accident, explosion) resulting in loss of consciousness
	CES-D	Self-reported depression symptoms
	DRRI Combat	Self-reported combat exposure
Self report outcome measures		
	Instrument	**Domain Assessed**
	MOS-CF	Self-reported impact of cognitive problems on daily functioning
	SF-12	Self-reported impact of health problems on daily functioning
Performance-based outcome measures		
	Instrument	**Domain Assessed**
Attention, working memory, executive functioning		
	NES3 CPT, omissions and false positives	Sustaining attention/vigilance over time; target detection
	Trailmaking	Working memory/executive functioning
	WMS3 Verbal Paired Associates (immediate and delayed)	Verbal-auditory learning
	WMS Visual Reproductions (immediate and delayed)	Visual-spatial memory over time
Reaction time		
	ANAM Simple Reaction Time	Reaction time to simple, recurring stimulus
Cognitive efficiency		
	ANAM code substitution, matching to sample, logical relations, mathematical processing, running memory	Efficiency in matching, recognition memory, reasoning, mental computation, and working memory
Motor performance		
	ANAM finger tapping, dominant and nondominant hands	Fine motor speed

Table 2. Standardized regression (beta) weights for mTBI, PTSD symptoms, depression symptoms and combat exposure as predictors of cognitive outcome and self-report of health and cognitive concerns.

	mTBI	**PCL**	**CES-D**	**DRRI**
Beta at:	**Step 4**	**Step 5**	**Step 5**	**Step 5**
Attention, Executive				
CPT, false +	-.029	.035	.045	.014
CPT, omissions	.04	**.097*** **	.065	.050
Math Processing	-.044	-.032	-.065*	-.035
Trails B-A (time to completion)	-.012	.019	.014	.028
Learning/Memory				
Visual Reproduction, immediate	-.054	**-.090*** **	**-.085*** **	045
Visual Reproduction, retention	-.076*!	-.090*	-.054	-.051
Verbal Paired Assoc., learning	-.015	**-.082*** **	**-.084*** **	-.027
Verbal Paired Assoc., retention	.000	-.016	-.038	-.046
Delayed Matched to Sample	.018	-.051	-.026	-.020
Code Substitution, immediate	.004	**-.089*** **	**-.088*** **	-.012
Code Substitution, delay	.014	**-.107*** **	**-.077*** **	-.048
Psychomotor				
Simple Reaction Time	-.041	**.121*** **	**.180*** **	.013
Finger Tapping, dominant	-.045	-.071*	-.080**	-.022
Finger Tapping, non-dominant	.009	-.078**	**-.081*** **	.052
Self Report				
Health problems	**-.114*** **$	**-.165*** **	**-.145*** **	-.011
Cognitive problems	-.012	**-.498*** **	**-.519*** **	-.087**

Note: * $p \leq .05$, ** $p \leq .01$, *** **$p \leq .005$**

! At Step 5 for both models, this beta becomes non-significant.

$ At Step 5 for both models, this beta remains significant.